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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,445	03/09/2001	Gary Van Nest	377882001300	7011

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,445	NEST ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,9-12,14 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,9-12,14 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-4, 6, 9-12, 14, and 23-27 are pending in the application.

2. In the prior action, mailed on January 24, 2006, claims 1-4, 6, 9-12, 14, and 23-26 were pending and rejected. In the Response of July 24, 2006, the Applicant presented additional arguments in traversal of the rejections.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on July 24, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. **(New Rejection- Based on IDS reference)** Claims 1-3, 6, 9-11, 14, and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating or delaying HPV associated lesions through administration of the ISS sequence of SEQ ID NO: 1, does not reasonably provide enablement for methods of doing so in any mammal wherein the ISS comprises either SEQ ID NO: 1 or any of the sequences within the

scope of (e.g.) claims 1-3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. The factors considered most relevant are the scope of the claims, the presence or absence of working examples, and the nature of the invention, and the predictability of unpredictability of the art.

In the present case, the claims are broadly drawn to the use of any oligonucleotide sequence (or of any sequence of between 6 and 200 bases in length) comprising the ISS sequences disclosed in the claims for the treatment or delaying of lesions associated with human papillomavirus (HPV) infection. In support of the claimed invention, the application has shown that the administration of the sequence of SEQ ID NO: 1 (22 bases in length) was effective for the claimed purposes.

However, the application does not demonstrate that any sequence comprising the shorter ISS sequences in claims 1-3, or that sequences consisting of such sequences would also be so

effective. Moreover, the art specifically teaches that "there has been no published report of ISS activity in human cells by" ISS sequences of less than 8 nucleotides in length. See e.g., Fearon et al., Eur J Immunol 33: 2114-22 (of record in the July 2004 IDS). See also, Verthelyi et al., I Immunol 166: 2372-77, at 2373 (indicating that the minimum length for a cytokine stimulating ISS is about 18 bases). The Fearon reference specifically teaches that the sequence ACGTTCG, varying from one of the sequences of claim 3 by only one base, and comprising the sequence claim 1, was inactive. Page 2115 (right column). In addition, the reference also teaches that ISS sequences wherein the sequence TCG is found in the ultimate or penultimate residues, such as in the case of the sequences of each of claims 1-3, of the sequence were also inactive.

The reference additionally teaches that not only is the minimal ISS motif required for effective activity, but also that additional structural requirements must also be met to ensure active ISS sequences. Page 2119, left column. The reference also teaches that the nature of the bases outside of the minimal hexamer is also important for activity. Id. Such teachings find support in the disclosure of Marshall et al. (DNA Cell Biol 24: 63-72- of record in the July 2004 IDS), which teaches that different ISS sequence structures result in ISS sequences that have different immunomodulating activities. Pages 63-64. Thus, the reference indicates that not every larger ISS sequence comprising the sequence motifs of claims 1-3 would be capable of inducing the required anti-HPV activity.

Moreover, the claims are also drawn to the induction of such anti-HPV activity in any mammal. The application shows that the sequence of SEQ ID NO: 1 is effective in mice. However, Verthelyi et al. (J Immunol 166: 2372-77- cited by Fearon et al.) teaches that different species respond to CpG sequences differently. Page 2372, left column. In particular, it is noted

that the reference teaches that humans respond poorly to the optimal ISS sequences of mice. These teachings thereby indicate that the fact that SEQ ID NO: 1 was an effective anti-HPV drug in mice does not necessarily demonstrate its anti-HPV activity in any mammal.

The art therefore indicates a limited knowledge in the art at the time the application was filed, and unpredictability in the art. Such teachings tend to indicate that the limited examples and guidance presented in the present application would not have enabled those of ordinary skill in the art to practice the claimed invention to the full extent as claimed. In view of these teachings, and because it is not clear what activity (and therefore structure) of the ISS of SEQ ID NO: 1 resulted in its anti-HPV effects, and in view of the limited working examples and guidance as to what other ISS sequences or what ISS motifs would result in an effective anti-HPV therapeutic, the claims are rejected as exceeding the scope for which an enabling disclosure has been provided.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. **(Prior Rejection- Maintained)** Claims 1-4, 6, 9-12, 14, and 23-26 were rejected under 35 U.S.C. 103(a) as being unpatentable over Beutner, Bauman, and Yamamoto, and further in view of either of Raz et al. (U.S. patent 6,514,948), and Schwartz et al. (WO 98/55495- of record in the Feb 2002 IDS). The claims are drawn to a method for delaying the development of, or

reducing the severity of, lesions caused by HPV infections through the administration of an immunostimulatory nucleic acid sequence to the site of the lesion or infection. The rejection is maintained, and extended to new claim 27.

The applicant provides a number of arguments in traversal of the rejection. First, the Applicant presents a number of arguments distinguishing the teachings of each of the cited references from the claimed invention. With respect to these arguments in traversal, it is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, each of the arguments presented by the Applicant fails to consider the teachings of at least one of the references. Thus, while the Examiner agrees that no one of the cited references provides sufficient teachings to render the claimed invention obvious, this is not considered relevant as the rejection is based not on the cited references individually, but on what those of ordinary skill in the art would have considered obvious based on the combination of these teachings. The Applicant's arguments are therefore not found persuasive.

It is noted that, while the Applicant asserts that the cited art does not teach particular dosages of the ISS sequences to correspond to the IFN-α used in the Beutner reference, there are no dosage requirements presented in the present claims. Further, it is considered to be within the realm of routine optimization for those of ordinary skill in the art to determine the optimum dosages of a drug to be administered to a patient. This argument is therefore not considered persuasive. The remaining assertions regarding the teachings of the prior art have bee addressed previously.

The Applicant also specifically asserts both that there is no motivation for the combination of the references, and no reasonable expectation of success in the combination. These arguments are, in part, based upon arguments of the deficiencies of the individual references, or certain combinations of the references. This argument is therefore not found persuasive for the reasons above. Motivation for the combination of the references was previously provided. The Applicant also asserts that those in the art would not have had a reasonable expectation of success on the basis of other assertions. However, it is noted that the Applicant has not provided any evidence in support of their assertions. The provision of attorney argument is not sufficient to overcome evidence. See e.g., MPEP § 716.01(b) and 2145 I. In the present case, as has been described previously, the prior art cumulatively teaches that certain ISS sequences were known to induce IFN-α production, and that IFN-α was known in the art for the treatment of HPV infections. Thus, it would have been obvious to those of ordinary skill in the art to have combined such teaches to result in the claimed method. The Applicant has not presented any evidence to the contrary.

Because the Applicant's arguments do not take into consideration the teachings of the cited references as a whole and are based on conclusions for which no evidence has been presented, they are not found persuasive. The rejection is therefore maintained for the reasons above, and for the reasons of record.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is

appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(Prior Rejection- Maintained) Claims 9-12, 14, 25, and 27 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 11 of copending Application No. 10/898,512. The Applicant presented no arguments in traversal of the rejection. Because the rejection is not being held in abeyance, the rejection is maintained for the reasons of record.

Conclusion

9. No claims are allowed.

10. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on July 24, 2006 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
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